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Intellectual Property
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EXAMINER

SMITH, CAROLYN L

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 11/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/966,870	BADER, JOEL S.	
	Examiner	Art Unit	
	Carolyn L Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 30 August 2004.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 25-27 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 25-27 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
	6) <input type="checkbox"/> Other: _____.

DETAILED ACTION

Applicant's amendments and remarks, filed 8/30/04, are acknowledged. Amended claims 25 and 27 are acknowledged.

Applicant's arguments, filed 8/30/04, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 25-27 are herein under examination.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The rejection of claims 25-27 is maintained under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter. This rejection is maintained and reiterated for reasons of record.

One interpretation of claim 25 step (a) is that the provision of single-nucleotide polymorphisms (SNPs) involves actual laboratory practice. Another interpretation is that all

steps of claim 25, including the step (a), are taking place on a computer. With this latter interpretation, the claims appear to lack any physical result performed outside of a computer.

As stated in MPEP § 2106, (IV)(B)(2)(b), to be statutory, a claimed computer-related process must either: (A) result in a physical transformation outside the computer for which a practical application in the technological arts is either disclosed in the specification or would have been known to a skilled artisan (discussed in MPEP § 2106 (IV)(B)(2)(b)(i)), or (B) be limited to a practical application within the technological arts (discussed in MPEP § 2106 (IV)(B)(2)(b)(ii)).

As stated in MPEP § 2106 (IV)(B)(2)(b)(i), the independent physical acts may be post- or pre-computer processing activity as described below:

A process is statutory if it requires physical acts to be performed outside the computer independent of and following the steps to be performed by a programmed computer, where those acts involve the manipulation of tangible physical objects and result in the object having a different physical attribute or structure. *Diamond v. Diehr*, 450 U.S. at 187, 209 USPQ at 8. Thus, if a process claim includes one or more post-computer process steps that result in a physical transformation outside the computer (beyond merely conveying the direct result of the computer operation), the claim is clearly statutory.

Another statutory process is one that requires the measurements of physical objects or activities to be transformed outside of the computer into computer data (*In re Gelnovatch*, 595 F.2d 32, 41 n.7, 201 USPQ 136, 145 n.7 (CCPA 1979) (data-gathering step did not measure physical phenomenon); *Arrhythmia*, 958 F.2d at 1056, 22 USPQ2d at 1036), where the data comprises signals corresponding to physical objects or activities external to the computer system, and where the process causes a physical transformation of the signals which are intangible representations of the physical objects or activities. *Schrader*, 22 F.3d at 294, 30 USPQ2d at 1459 citing with approval *Arrhythmia*, 958 F.2d at 1058-59, 22 USPQ2d at 1037-38; *Abele*, 684 F.2d at 909, 214 USPQ at 688; *In re Taner*, 681 F.2d 787, 790, 214 USPQ 678, 681 (CCPA 1982).

As stated in MPEP § 2106 (IV)(B)(2)(b)(ii), the computer-related process may be limited to a practical application in the technological arts as described below:

There is always some form of physical transformation within a computer because a computer acts on signals and transforms them during its operation and changes the state of its components during the execution of a process. Even though such a physical transformation occurs within a computer, such activity is not determinative of whether the process is statutory because such transformation alone does not distinguish a statutory computer process from a nonstatutory computer process. What is determinative is not how the computer performs the process, but what the computer does to achieve a practical application. See *Arrhythmia*, 958 F.2d at 1057, 22 USPQ2d at 1036.

Claims 25-27 do not fulfill either of these statutory requirements and are therefore rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter.

The rejection of claims 25-27 is maintained under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter. This rejection is maintained and reiterated for reasons of record.

As written, the claims appear to be directed to a method that merely manipulates numbers, abstract concepts or ideas, or signals representing any of the foregoing.

As stated in MPEP § 2106, (IV)(B)(1), if the “acts” of a claimed process manipulate only numbers, abstract concepts or ideas, or signals representing any of the foregoing, the acts are not being applied to appropriate subject matter. Schrader, 22 F.3d at 294-95, 30 USPQ2d at 1458-59. Thus, a process consisting solely of mathematical operations, i.e., converting one set of numbers into another set of numbers, does not manipulate appropriate subject matter and thus cannot constitute a statutory process.

In practical terms, claims define nonstatutory processes if they:

- consist solely of mathematical operations without some claimed practical application (i.e., executing a “mathematical algorithm”); or
- simply manipulate abstract ideas, e.g., a bid (Schrader, 22 F.3d at 293-94, 30 USPQ2d at 1458-59) or a bubble hierarchy (Warmerdam, 33 F.3d at 1360, 31

USPQ2d at 1759), without some claimed practical application.

Claims 25-27 do not fulfill any of these statutory requirements and are therefore rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter.

Applicant argues that claim 25 does not mention a “computer” and that step (a) of this claim is clearly not performed on a computer. These statements are found unpersuasive, because even though the term “computer” is not in the claim, a broad and reasonable interpretation of this claim is that the steps are performed on a computer, including step (a), regardless of what the working examples state. Applicant states a computer cannot “provide” a plurality of SNPs and haplotypes. This statement is found unpersuasive as a computer can provide a plurality of SNPs and haplotypes from data already stored on the computer. Applicant states the method is directed to a method for determining whether a genetic region is associated with responsiveness to an agent that is well known to have healthcare applications. This statement of association appears to be a further characterization of data without specifically mentioning what practical application it will be used for, such as detecting disease, finding lead drugs, and other practical applications found outside of the computer.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is necessitated by amendment.

Applicant cites page 19 (line 12) to page 22 (line 20) of the specification to provide support for the amendments in claim 25, including “determining whether … is” in lines 1-2 and the penultimate line. The above-mentioned section of the specification mentions association studies including polymorphisms already associated with response to agents in published literature (page 19, lines 20-30). Therefore, this does not appear to be determining whether a genetic region is associated with responsiveness to an agent as such determination has already been made. Because the introduction of “determining whether… is” appears to lack support in the specification, claims, and/or drawings, as originally filed, this phrase is considered to be NEW MATTER. Claims 26-27 are also rejected due to their dependency from claim 25. This rejection is necessitated by amendment.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

LACK OF ENABLEMENT

The rejection of claims 25-27 is necessitated by amendment under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This rejection is modified as necessitated by amendment.

Claim 25 recites steps (a)-(d) that provides single-nucleotide polymorphisms (SNPs) and haplotypes, identifies SNPs in a linkage disequilibrium, compares these SNPs to haplotypes, and then selects a correlation test to determine whether a genetic region is associated with responsiveness to an agent. Because steps other than step (a) do not necessarily keep the quantities of data separate between chromosomal regions, this lack of separation would make it

difficult for one of skill in the art to be able to make and use this invention which seeks to determine whether a single genetic region is associated with responsiveness to an agent. Claim 25 does not address the scenario that more than one genetic region may form such an association. To perform such a method, it appears that one of skill in the art would need to analyze any correlation test that was selected as well as use a threshold or other statistical parameter to scientifically conclude that the probability of an association significantly occurs rather than by merely selecting a correlation test and then jumping to the conclusion of region association determination, as stated in instant claim 25. Therefore, the steps recited in claim 25 do not appear to enable one of skill in the art to determine whether a genetic region is associated with responsiveness to an agent.

Applicant states claim 25 has been amended such that only one genetic region is concerned at a time. This statement is found unpersuasive as multiple chromosomal regions (which are reasonably and broadly interpreted to be genetic regions) are mentioned in step (a) which suggests multiple genetic regions are being used in the instant method.

Claims Rejected Under 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejections of claim 25 are maintained and necessitated by amendment under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claim 25, lines 1 and 14, recites the phrase “associated with” which is vague and indefinite. It is unclear which parameters and to what degree these parameters must be met to be considered to be associated. Clarification of the metes and bounds of the claim via clearer claim wording is requested. Claims 26-27 are also rejected due to their dependency from claim 25.

This rejection is maintained.

Applicants cite the specification (page 3, first paragraph) which explains a p-value less than a predetermined limit to establish association. This paragraph also mentions a p-value provides the probability that the association of the phenotype with a particular set is due to random association. It is noted that claim 25 does not mention p-values or whether this recited association is considered to be random or statistically significant. It is noted that the method steps in claim 25 stop after selecting a correlation test without actually performing or analyzing the test. Therefore, the phrase “associated with” as stated in instant claim 25 is still considered to be vague and indefinite.

Claim 25, penultimate line, recites the phrase “said genetic region” which lacks proper antecedent basis. The preamble mentions only one genetic region; however step (a) mentions one or more regions of a chromosome that represent multiple genetic regions. Therefore, it is unclear if the “said genetic region” in the penultimate line is supposed to exclude all but one of the previously mentioned chromosomal regions, as stated in step (a) of the instant claim. Claims

26-27 are also rejected due to their dependency from claim 25. This rejection is necessitated by amendment.

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejection of claims 25-27 is maintained under 35 U.S.C. 102(e)(2) as being anticipated by Drysdale et al. (P/N 6,586,183 B2).

Because the introduction of “*determining whether* a genetic region is associated with responsiveness to an agent” is considered NEW MATTER that needs to be removed from instant claim 25, this determination phrase was not considered in the prior art.

This rejection is maintained and reiterated for reasons of record.

Drysdale et al. disclose a method for identifying a genetic region associated with responsiveness to β -agonists (agents) (abstract and col. 3, lines 25-36 and line 52 to col. 4, line 5). Drysdale et al. disclose a plurality of single-nucleotide polymorphisms (SNPs) in a particular region (col. 1, lines 30-67). Drysdale et al. disclose the identity of several of the polymorphic sites that are reported to be in linkage disequilibrium in a particular gene (region) (col. 2, lines

34-42). Drysdale et al. disclose a number of haplotypes for this region (col. 2, lines 42-59 and col. 4, lines 24-32). Drysdale et al. disclose determining whether additional polymorphisms exist (other regions) and how such polymorphisms are combined in different copies of the gene to haplotypes (col. 3, lines 25-36 and col. 5, lines 30-38) which represents the comparison step (c) of instant claim 25. Drysdale et al. disclose performing haplotyping methods on other genomic regions (col. 19, lines 50-53). Drysdale et al. disclose using various correlation techniques between a treatment and haplotypes and polymorphic sites, including regression tests and ANOVA (col. 22, lines 30-31 and col. 23, lines 7-25 and col. 24, lines 21-58). Drysdale et al. disclose analyzing haplotypes with an analysis of covariance model (ANCOVA) (haplotype-based correlation test) SNPs with an ANCOVA model (SNP-based correlation test) (col. 31, lines 1-23). Drysdale et al. disclose performing regression to determine the minimal number of polymorphisms that predict association between the polymorphisms and response to albuterol (agent) (col. 32, lines 37-40). The regression calculations created groups between haplotypes or SNPs based on response (col. 32, lines 37-45). Drysdale et al. disclosed testing sites independently (SNP-based regression) and combining sites that showed nominal association into haplotypes (haplotype-based regression) while discarding certain haplotypes with weaker associations (col. 32, lines 45-57) which represents a test selection depending on the number of SNPs in linkage disequilibrium being more or less than the number of haplotypes, as stated in instant claim 25.

Thus, Drysdale et al. anticipate the instant invention.

Applicant argues that Drysdale et al. do not teach step (d) of instant claim 25, because Drysdale et al. do not teach how to choose a correlation test. Applicant states Drysdale et al. describe a laundry list of correlation tests that can be used in analyzing haplotypes. According to the online Merriam-Webster's dictionary, "select" is defined as choosing from a number or group, which is precisely what Drysdale et al. do regarding correlation tests. Drysdale et al. disclose using various correlation techniques, including the two listed in instant claims 26 and 27 (see prior art discussion above). The fact that Drysdale et al. used these techniques clearly demonstrates that they were selected in their invention. Thus, Applicant's arguments are deemed unpersuasive.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

November 1, 2004

Ardin H. Marschel 11/1/04
ARDIN H. MARSCHEL
PRIMARY EXAMINER